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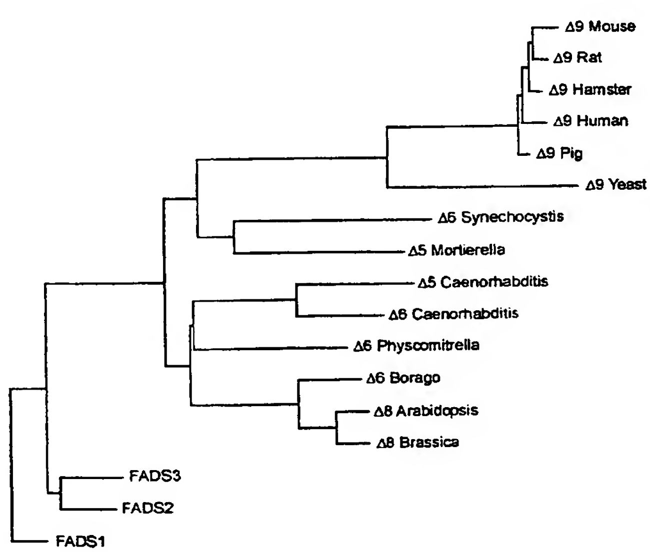
(54) cDNA molecules of the members of gene family encoding human fatty acid desaturases and their use in diagnosis and therapy

(57) The present invention relates to the cloning and sequencing of the cDNA molecules of three members of a gene family encoding three human fatty acid desaturases, fatty acid desaturase-1 (FADS 1), fatty acid desaturase-2 (FADS2) and fatty acid desaturase-3 (FADS3). The invention also relates to diagnostic methods of screening for and detection of FADS1, FADS2, FADS3 and gene therapy utilizing recombinant DNA as well as the generation of animal models (knock-in, knock-out, transgenic animals), anti-FADS1, anti-FADS2, anti-FADS3 antibodies and use in screenings for modulating drugs.

Fig.2



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Description

Field of the invention

[0001] The present invention relates to the cloning and sequencing of the cDNA molecules of three members of a gene family encoding three human fatty acid desaturases, fatty acid desaturase-1 (FADS1), fatty acid desaturase-2 (FADS2) and fatty acid desaturase-3 (FADS3). The invention also relates to diagnostic methods of screening for and detection of FADS1, FADS2, FADS3 and gene therapy utilizing recombinant DNA as well as the generation of animal models (knock-in, knock-out, transgenic animals), anti-FADS1, anti-FADS2, anti-FADS3 antibodies and use in screenings for modulating drugs.

Background of the Invention

[0002] Cellular membranes are dynamic structures in which variable amounts of proteins are embedded in a lipid bilayer whose hydrophobic characteristics are largely due to fatty acid moieties of complex lipids (Singer and Nicolson 1972). The 'fluidity' of the membranes are achieved by incorporating unsaturated fatty acyl chains of varying lengths and varying degrees of unsaturation into the lipids (Stubbs and Smith 1984). In animals, some of the unsaturated fatty acids need to be supplied by the diet ('essential polyunsaturated fatty acids') but, in part, can also be synthesized de novo by oxidative desaturation (i.e. formation of double bonds) of saturated fatty acids of plant and animal origin. Polyunsaturated fatty acid formation requires acetyl-CoA dependent chain elongation and desaturation. Most mammalian tissues can modify acyl chains by introducing more than one double bond with the first one generally at the Δ-9 position between carbons C-9 and C-10. Subsequent double bonds may then be inserted at the Δ-4, Δ-5, and Δ-6 positions by individual desaturase activities (Cook 1991).

[0003] For the two major precursors of the (n-6) and (n-3) series of polyunsaturated fatty acids, linoleic 18:2(n-6) and alpha-linolenic 18:3(n-3) acids, animals depend entirely on their dietary intake. By alternating sequences of desaturation (involving the subsequent action of Δ4, Δ5- and Δ6-desaturases, respectively) and C2 chain elongation, linoleic and alpha-linolenic acids are utilized to form arachidonic acid, 20:4(n-6), and the (n-3) acyl chains eicosapentaenoic acid, 20:5(n-3), and docosahexaenoic acid, 22:6(n-3), respectively (Cook 1991).

[0004] Linoleic and arachidonic acid are the only members of the (n-6) family that accumulate in large quantities in liver and most other animal tissues. The intermediates 18:3(n-6) and 20:3(n-6) are formed from 18:2(n-6) by Δ6-desaturation, chain elongation and Δ5-desaturation (Horrobin 1993). As a component of phospholipids arachidonic acid is abundant in cellular membranes but also serves as the primary precursor of oxygenated derivatives such as prostaglandine E2 which is pro-inflammatory and regulates cell function of the immune system.

[0005] The (n-3) acyl chains eicosapentaenoic acid [20:5(n-3)] and docosahexaenoic acid (22:6(n-3)] are most abundant in cerebral cortex, retina, and spermatozoa. Although it is generally assumed that the liver is the major source of 22:6(n-3), it has been shown that docosahexaenoic acid can also be produced by retinal pigment epithelium (Wang and Anderson 1993) as well as brain astrocytes (Moore et al. 1991, Delton-Vandenbrouke et al. 1997). In retinal rod outer segments, phospholipids may contain 40-60% of 22:6(n-3) which can markedly influence membrane fluidity due to the presence of six double bonds.

[0006] In recent years there has been increasing interest in the role of polyunsaturated fatty acids in the pathobiology of a number of chronic conditions such as coronary and peripheral vascular disease (Horrobin 1995), acute and chronic inflammatory immune responses (Calder 1998, Fan and Chapkin 1998, Grimble and Tappia 1998), cutaneous abnormalities (Horrobin 1989. Grattan et al. 1990), essential hypertension (Russo et al. 1997, Chi and Gupta 1998), diabetes mellitus (Mori et al. 1997), asthma (Leichsenring et al. 1995, Villani et al. 1998, Hodge et al. 1998) and rheumatoid arthritis (James and Cleland 1997, Ariza-Ariza et al. 1998, Grimble and Tappia 1998). A particular role has been attributed to gamma-linolenic acid [18:3(n-6)] as an anti-cancer polyunsaturated fatty acid. It has been shown that 18:3 (n-6) confers anticancer properties by a variety of mechanisms such as (i) up-regulation of E-cadherin, a cell-cell adhesion molecule which acts as a suppressor of metastasis (Jiang et al. 1995), (ii) regulation of desmosome-mediated cell-cell adhesion in human cancer cells (Jiang et al. 1997a), (iii) up-regulation of the metastasis-suppressor gene nm-23 thus contributing to the inhibition of the in vitro invasion of tumor cells (Jiang et al. 1998a), (iv) up-regulation of maspin expression, a mammary serine protease inhibitor, with profound effects on motility of cancer cells (Jiang et al. 1997b) and (v) finally inhibition of cell cycle progression via regulation of phosphorylation and subsequent degradation of cell cycle inhibitors p27kip1 and p57kip2 (Jiang et al. 1998b).

[0007] To further understand lipid-related function in human health and disease additional research into fatty acid biosynthesis and metabolism is required. In particular, we need to understand the pharmacological properties, the mechanisms of action and the tissue-specific regulation of composition of the polyunsaturated fatty acids and their metabolites. This will provide additional insight into the role of the polyunsaturated fatty acids in various chronic disease states and will make it feasible to focus pharmacogenomic research on drug design and valuation with the goal of

ameliorating acute health problems associated with impaired lipid function. As a prerequisite, the genes and their gene products involved in the above-mentioned processes need to be identified and characterized.

[0008] It is the objective of the present invention to provide cDNA molecules of three novel members of the human membrane fatty acid desaturase gene family, termed FADS1, FADS2 and FADS3. The thr e genes share a nucleic acid identity of approximately 50-60% and an amino acid identity of about 77% with each other. Similar to other membrane-bound desaturases from mammals, fungi, insects, plants and cyanobacteria FADS1, FADS2 and FADS3 reveal a hydropathy profile typical of membrane-bound desaturases and share three regions of highly conserved primary sequence of the general histidine motif $HX_{2(3)}$[XH]H (Shanklin et al. 1994). The histidine residues may act as metal-chelating ligands involved in the binding of oxygen in the reaction center (Shanklin et al. 1995). Together, these features confirm FADS1, FADS2 and FADS3 as novel members of the desaturase family of fatty acyl chain-modifying enzymes.

[0009] Amino acid identity of FADS1, FADS2 and FADS3 to known desaturases (e.g. from *Arabidopsis thaliana, Brassica napus, Synechocystis spec., Borago officinalis, Helianthus annuus, Saccharomyces cerevisiae* and *Caenorhabditiselegans*) is restricted to the respective carboxy terminal regions (amino acid positions 260 to 422) revealing an overall sequence identity of approximately 27%. Interestingly, the respective amino-termini of the three novel proteins demonstrate similarities to cytochrome b5 (amino acid positions 4 to 75; Fig. 1). Cytochrome b5 is a small hemoprotein and functions as an intermediate donor in a number of oxidation/reduction reactions including e.g. the NADH-dependent Δ9 stearoyl-CoA desaturation (Strittmatter et al. 1974) or the Δ5 desaturation in cholesterol biosynthesis (Reddy et al. 1977). From the amino acid alignments we conclude that FADS1, FADS2 and FADS3 are fusion proteins consisting of a N-terminal cytochrome b5 and a C-terminal desaturase-like enzyme. From a functional point of view, this fusion of two activities may increase the efficiency of electron transport required for desaturation by covalently bringing together the presumed electron donor (cytochrome b5) and its putative acceptor (desaturase-like enzyme). Other heme fusion proteins containing the cytochrome b5 domain have been identified and represent a superfamily of fused proteins (Guiard and Lederer 1979). Besides others this superfamily includes the yeast flavocytochrome b_2, sulfite oxidase, nitrate reductase, the yeast Δ9 acyl-CoA desaturase and more recently the sunflower cytochrome b5-desaturase fusion protein (Sperling et al. 1995). The three novel desaturase-like enzymes reported herein, FADS1, FADS2 and FADS3, can be added to the growing list of members of this superfamily of fused proteins (Fig. 2).

Summary of the invention

[0010] The eukaryotic fatty acid desaturases represent a group of iron-containing enzymes that catalyze NAD(P)H- and O_2-dependent introduction of double bonds into fatty acyl chains. Impairment of desaturase activities has been implicated in a variety of human conditions including liver disease, coronary artery disease and cancer. With the present invention we are providing three isolated human cDNA molecules that encode three novel members of a cytochrome-b5-containing fusion protein with similarity to plant and lower animal desaturase enzymes, termed fatty acid desaturase-1 (FADS1) (represented by Fig. 3 and SEQ ID NO. 1), fatty acid desaturase-2 (FADS2) (represented by Fig. 4 and SEQ ID NO. 2) and fatty acid desaturase-3 (FADS3) (represented by Fig. 5 and SEQ ID NO. 3).

FADS1 protein

[0011] MAPDPVAAETAAQGPTPRYFTWDEVAQRSGCEERWLVIDRKVYNISEFTRRHPGGS RVISHYAGQDATDP-
FVAFHINKGLVKKYMNSLLIGELSPEQPSFEPTKNKELTDEFREL RATVERMGLMKANHVFFLLYLLHILLLDGAAWLTL-
WVFGTSFLPFLLCAVLLSAVQAQA GWLQHDFGHLSVFSTSKWNHLLHHFVIGHLKGAPASWWNHMHFQHHAKPNC-
FRKD PDINMHPFFFALGKILSVELGKQKKKYMPYNHQHKYFFLIGPPALLPLYFQWYIFYFVIQ RKKWVDLAWMITFY-
VRFFLTYVPLLGLKAFLGLFFIVRFLESNWFVWVTQMNHIPMHID HDRNMDWVSTQLQATCNVHKSAFNDWFSGHL-
NFQIEHHLFPTMPRHNYHKVAPLVQ SLCAKHGIEYQSKPLLSAFADIIHSLKESGQLWLDAYLHQ

FADS2 protein

[0012] MGKGGNQGEGAAEREVSVPTFSWEEIQKHNLRTDRWLVIDRKVYNITKWSIQHPGG QRVIGHYAGEDAT-
DAFRAFHPDLEFVGKFLKPLLIGELAPEEPSQDHGKNSKITEDFRA LRKTAEDMNLFKTNHVFFLLLLAHIIALESIA-
WFTVFYFGNGWIPTLITAFVLATSQAQAG WLQHDYGHLSWRKPKWNHLVHKFVIGHLKGASANWWNHRHFQHH-
AKPNIFHKDPD VNMLHVFVLGEWQPIEYGKKKLKYLPYNHQHEYFFLIGPPLLIPMYFQYQIIMTMIVHKN WVDLA-
WAVSYYIRFFITYIPFYGILGALLFLNFIRFLESHWFVdNTQMNHIVMEIDQEAY RDWFSSQLTATCNVEQSFFNDWFS-
GHLNFQIEHHLFPTMPRHNLHKIAPLVKSLCAK HGIEYQEKPLLRALLDIIRSLKKSGKLWLDAYLHK

FADS3 protein

[0013] MGGVGEPGPREGPAQPGAPLPTFCWEQIRAHDQPGDKWLVIERRVYDISRWAQRHP GGSRLIGHHGAEDATDAFRAFHQDLNFVRKFLQPLLIGELAPEEPSQDGPLNAQLVED FRALHQAAEDMKLFDASPTFFAFLLGHILAMEVLAWLLIYLLGPGWVPSALAAFILAISQ AQSWCLQHDLGHASIFKKSWWNHVAQKFVMGQLKGFSAHWWNFRHFQHHAKPNIF HKDPDVTVAPVFLLGESSVEYGKKKRRYLPYNQQHLYFFLIGPPLLTLVNFEVENLAY MLVCMQWADLLWAASFYARFFLSYLPFYGVPGVLLFFVAVRVLESHWFVWITQMNHI PKEIGHEKHRDWVSSQLAATCNVEPSLFTNWFSGHLNFQIEHHLFPRMPRHNYSRVA PLVKSLCAKHGLSYEVKPFLTALVDIVRSLKKSGDIWLDAYLHQ

[0014] Studies to clarify the specificity and the subcellular location of these ubiquitiously expressed fusion proteins are in progress. Also, the detailed cellular functions and dysfunctions of the desaturase-like domains are being investigated in appropriate cellular and animal systems. This will address the question whether and to which extent these novel enzymes are involved in human disease. The invention encompasses the three cDNA molecules, FADS1, FADS2, and FADS3, the nucleotide sequence of these cDNAs, and the putative amino acid sequences of the FADS1 (represented by Fig. 6 and SEQ ID NO. 4), FADS2 (represented by Fig. 7 and SEQ ID NO. 5), and FADS3 represented by Fig. 8 and SEQ ID NO. 6) proteins.

[0015] Also comprehended by this invention are oligonucleotide primers comprising the cDNA molecule or its complementary strand allowing the amplification of FADS1 (represented by Fig. 9 and SEQ ID NOS. 7-12), FADS2 (represented by Fig. 9 and SEQ ID NOS. 13-18), and FADS3 (represented by Fig. 9 and SEQ ID NOS. 19-22), by the reverse transcriptase polymerase chain reaction (RT-PCR). Such primers are particularly useful and will provide researchers and physicians with an enhanced ability to assess the role of FADS1, FADS2, and FADS3 in human disease. The present invention also relates to methods of screening for and detection of FADS1, FADS2, and FADS3 mutation carriers including prenatal FADS1, FADS2, and FADS3 screening and diagnosis.

[0016] Having provided the isolated human FADS1, FADS2, and FADS3 cDNA sequences, also comprehended by this invention are the FADS1, FADS2, and FADS3 proteins, and derivatives thereof, in aspects of diagnosis and treatment of human disease. Finally, the invention pertains to proteins which comprise the same or substantially the same amino acid sequence (at least 200 amino acids) as that represented by Figs. 6, 7, 8 and SEQ ID NOS. 4, 5, 6 or a variant of the amino acid sequences having a deletion, addition or substitution of 1 to 10 amino acids, or its salt.

[0017] Another aspect of the invention is the use of the FADS1, FADS2, and FADS3 proteins as a target for drug and gene therapy in the treatment of human disease. This includes the generation and utilization of FADS1, FADS2, and FADS3-targeted animal models (knock-in, knock-out, transgenic animals) and anti-FADS1, -FADS2, and -FADS3 antibodies that specifically detect the FADS1, FADS2, and FADS3 proteins, respectively.

[0018] The foregoing and other features and advantages of the invention will become more apparent from the following detailed description and accompanying drawings.

[0019] One aspect of the invention are the isolated cDNAs selected from the group consisting of:

(a) a polynucleotide having at least a 65 % homology, preferably at least a 80 % homology with a polynucleotide encoding a polypeptide selected from the group consisting of the polypeptides of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6;
(b) a polynucleotide having at least a 65 % homology, preferably at least a 80 % homology with a polynucleotide which by virtue of the redundancy of the genetic code, encodes the same polypeptide selected from the group consisting of the polypeptides of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6;
(c) a DNA molecule capable of hybridization under stringent conditions to a DNA molecule according to (a) or (b);
(d) a polynucleotide which is complementary to the polynucleotide of (a), (b) or (c); and
(e) a oligonucleotide comprising at least 15 consecutive nucleotides of the polynucleotide of (a), (b), (c) or (d)

(including DNAs which are synonymous to the DNAs of (a), (b), (c), (d) and (e) due to the degeneracy of the genetic code)
especially isolated cDNAs selected from the group consisting of:

(a) a polynucleotide having at least a 65 % homology, preferably at least a 80 % homology with a polynucleotide sequence selected from the group consisting of the polynucleotides of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3.
(b) a DNA molecule capable of hybridization under stringent conditions to a DNA molecule according to (a);
(c) a polynucleotide which is complementary to the polynucleotide of (a) or (b);
(d) a oligonucleotide comprising at least 15 consecutive nucleotides of the polynucleotide of (a), (b) or (c); and
(e) a DNA which is synonymous to the DNAs of (a), (b), (c) or (d) due to the degeneracy of the genetic code.

[0020] In the scope of the invention are polynucleotides having a polynucleotide encoding a polypeptide s lected

from the group consisting of the polypeptides of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3 and polynucleotides having a polynucleotide sequence selected from the group consisting of the polynucleotides of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, but DNAs comprising a nucleotide sequence with at least a 65 % homology with these nucleotide sequences is also within the scope of the invention.

[0021] Furthermore within the scope of th invention are:

[0022] A recombinant vector comprising the disclosed DNA molecules.

[0023] Transgenic host cells such as COS7, fibroblast cell lines or any other tissue-specific cell lines, as well as a transgenetic host cell tranformed by the DNA or the vector, a corresponding transgenetic organism or a corresponding transgenetic knock-in or knock-out animal model.

[0024] Polypeptides and corresponding proteins comprising at least 65 %, preferably 85 %, especially 100 % of a polypeptide sequence selected from the group consisting of the polypeptides of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3; polypeptides comprising a polypeptide sequence with at least a 65 % homology with the said polypeptides; peptides comprising at least 15, preferably 30, especially 60 consecutive amino acids of the said polypeptides; and polypeptides having substantially the same amino acid sequence as the said polypeptides, or having a variant of the amino acid sequence of the polypeptides with a deletion, addition or substitution of 1 to 10 amino acids. The salts of the peptides and proteins are also within the scope of the invention.

[0025] A process for preparing the proteins which comprises cultivating the transformants to form the proteins.

[0026] A method of screening for modulators in well known assays using constructs such as FADS1, FADS2, and FADS3 promoter luciferase or green fluorescent protein hybrids or screening for interacting proteins or factors using state of the art technologies like the interaction trap technology to screen for interacting substances of FADS1, FADS2, and FADS3 or isolated domains of FADS1, FADS2, and FADS3.

A method of screening chemical libraries comprising transformed cell lines

[0027] A compound which alters 1 reacts with at least one epitope of the proteins and which is obtained by screening methods utilizing the FADS1, FADS2, and FADS3 cDNAs or protein molecules.

[0028] Use of antibodies against the FADS1, FADS2, and FADS3 proteins for diagnostic or therapeutic purposes.

[0029] A pharmaceutical composition comprising as an effective component of the proteins or a partial peptide of the proteins, and a pharmaceutically acceptable carrier or diluent.

[0030] The term "knock-out animal" as used herein is intended to describe an animal containing a gene which has been modified by homologous recombination. The homologous recombination event may completely disrupt the gene such that a functional gene product can no longer be produced (hence the name "knock-out") or the homologous recombination event may modify the gene such that an altered, although still functional, gene product is produced.

[0031] The term "knock-in" as used herein is intended to describe a variation of gene targeting that uses homologous recombination but allows expression of added genetic sequences in place of the endogenous gene. This approach allows the test of more subtle mutations than is allowed by a simple knock-out.

[0032] The term "epitope" describes a region on a macromolecule which is recognized by an antibody. Frequently it is in a short region of primary sequence in a protein and it is generally about 5 to 12 amino acids long (the size of the antigen binding site on an antibody). Carbohydrates, nucleic acids and other macromolecules may be antigens and have epitopes.

Detailed Description of the Invention

Materials and Methods

[0033] Isolation of the FADS1 and FADS2 cDNAs cDNA fragments corresponding to FADS1 and FADS2 were identified by direct cDNA selection. The cDNA selection was performed essentially as described (Rommens et al. 1993) with only minor modifications. Briefly, total RNA was prepared from human retina and from established human retinal pigment epithelium cell line ARPE-19 (Dunn et al. 1996). Prior to the use as templates for cDNA synthesis the isolated RNAs were separated on a 1.2% agarose gel in the presence of 3-(*N*-morpholino)propanesulfonic acid (MOPS) and formaldehyde to check their integrity (Sambrook *et al.,* 1989).

[0034] RNAs were reverse transcribed using the SUPERSCRIPT™ preamplification system for first strand cDNA synthesis (Gibco, BRL) and the $RXGT_{12}$ oligonucleotide primer (5'-CGG AAT TCT CGA GAT CTT TTT TTT TTT TT-3'). After poly(A)-tailing with terminal transferase (United States Biochemical, USB), a cDNA pool was generated by $RXGT_{12}$-primed PCR at 94°C for 1 min; 2 cycles of 94°C, 30 sec; 37°C, 1 min, 72°C, 2 min followed by 22 cycles of 94°C, 30 sec; 58°C, 30 sec and 72°C, 2 min. Prior to hybridization the cDNA pools were pre-annealed to C_0t-1 DNA (Gibco, BRL) enriched with sonicated LINE1 sequences.

[0035] Genomic PAC clones for cDNA selection were derived from 11q12-q13.1, a region known to contain the gene

underlying Best's vitelliform macular dystrophy (Stöhr et al. 1998). The assembly and orientation of the clones have been described previously (Cooper et al. 1997). Inserts from PAC clones dJ465G21 and dJ139E20 (~1 µg) were isolated by NotI digestion, purified using QIAEXII agarose gel extraction beads (Qiagen) and immobilized on Hybond-N+ membrane filters with an average concentration of 60 ng/mm². The insert filters were subjected to two consecutive rounds of hybridization with a starting mixture of 20 µg of retina and ARPE-19 derived cDNAs. Hybridization time was four days at 58°C in Church hybridization buffer (Church and Gilbert 1984). Filters were washed three times in 2 x SSC/0.1% SDS at room temperature, once each in 0.5 x SSC/0.1% SDS, 0.2 x SSC/0.1% SDS and 0.2 x SSC/0.05% SDS (all at 58°C). A final wash was in 2 x SSC. cDNAs were eluted in distilled H_2O by incubating for 10 min at 98°C and reamplified by PCR using the $RXGT_{12}$ oligonudeotide primer. Four µg of the reamplified cDNAs were used for a second round of hybridization. After two rounds of selection the cDNAs were amplified using the $RXGT_{12}$ oligonucleotide primer, digested with EcoRI and cloned into the EcoRI site of pBluescript (Stratagene).

[0036] The selected cDNAs represent segments of the 3'-untranslated region (3'-UTR) of FADS1 (clone IVC4 at FADS1 nucleotide position 3793-4204; clone IVB7 at nucleotide position 3132-3609; done VIIC6 at nucleotide position 2077-2317) (Fig. 3) and of the 3' UTR/coding sequence of FADS2 (done IVB8 at FADS2 nucleotide position 2626-3009; clone TUK8-4B at nucleotide position 753-1508) (Fig. 4).

[0037] Using the selected clone sequences extensive dbEST database searches were conducted and revealed a large number of additional overlapping expressed sequence tags (ESTs). More than 100 ESTs (e.g. zk09h08, EST177650, yb28c03, ym29b05, yx67h05) were assembled to an overlapping EST contig representing FADS1. The assembled EST sequences contain an open reading frame (ORF) of 1410 bp, with a first potential in-frame translation initiation codon, ATG, starting 79 nucleotides downstream the most 5'end of EST clone zk09h08.r1 (GenBank acc. no. AA029030) (Fig. 1a). A consensus polyadenylation signal, AAUAAA, was identified at nucleotide position 4.182. The mature protein predicted from the ORF consists of 444 amino acid residues resulting in a calculated molecular mass of 52.0 kDa (Fig. 6).

[0038] Another 30 overlapping ESTs (e.g. cp2485.seq, HSC2EA121, EST06759, ym42c04, nc08c05) were found facilitating the assembly of the FADS2 cDNA. The assembled EST sequences contain an open reading frame (ORF) of 1352 bp, with a first potential in-frame translation initiation codon, ATG, starting 21 nucleotides downstream the most 5'end of EST done ub64e01.r1 (GenBank acc. no. AI036465) (Fig. 4). Consensus polyadenylation signals were predicted at nucleotide positions 2.996 and 4.056. The mature FADS2 protein predicted from the ORF consists of 444 amino acid residues resulting in a calculated molecular mass of 52.3 kDa (Fig. 7). Amino acid sequence identity between FADS1 and FADS2 is 62%.

Isolation of the FADS3 cDNA

[0039] Additional 30 human EST clones were available to assemble a third individual cDNA, termed FADS3 (e.g. zs84e06, zs84e05, nq23f05, ya49a19, zs86h09). The existence of a third member of the FADS family was confirmed by PCR mapping of FADS1-, FADS2- and FADS3-specific 3'-UTR fragments revealing three distinct gene loci within a 1.4 Mb PAC contig in 11q12-q13.1 (Cooper *et al.,* 1997). The assembled EST sequences contain an open reading frame (ORF) of 1468 bp, with a first potential in-frame translation initiation codon, ATG, starting 134 nucleotides downstream the most 5'end of EST clone qa99d06.s1 (GenBank acc. no. AI123992) (Fig. 5). The mature protein predicted from the ORF consists of 445 amino acid residues resulting in a calculated molecular mass of 51.2 kDa (Fig. 8). The 3'-UTR of the FADS3 cDNA is represented by several EST clones (e.g. zs86h09.s1, AA279632). A potential polyadenylation signal, AUUAAA, is present at cDNA nucleotide position 1.757 and may be functional as AUUAAA is the most common natural variant of the consensus polyadenylation signal AAUAAA (Fig. 5) (Sheets *et al.,* 1990).

[0040] Amino acid sequence identities between FADS1 and FADS3 as well as between FADS2 and FADS3 are 52% and 63%, respectively. All EST sequences in the dbEST databases could be aligned to one of the three cDNAs, FADS1, FADS2, and FADS3. This suggests that there are no additional members of the FADS family in the human genome.

Northern blot analysis

[0041] Northern blot analysis was performed either with total RNA isolated using the guanidinium thiocyanate method (Chomczynski and Sacchi 1987) or with commercially available multiple tissue Northem (MTN) blots purchased from Clontech Laboratories Inc. (Palo Alto, CA). Each lane of the total RNA blot contained 12 µg of total RNA from lung, cerebellum, uterus, retina, liver, heart, RPE cell line ARPE-19, RPE tissue, lymphocytes and was electrophoretically separated in the presence of formaldehyde. The MTN blots were prepared from poly(A)$^+$ RNA isolated from human heart, brain, placenta, lung, liver, skeletal muscle, kidney and pancreas. Inserts of clones IVC4, IVB7 (FADS1), IVB8 (FADS2) and of the 362 bp PCR product F3/R (5'-ACAGCTTTCCCCCAATTCTC-3'/5'-GGCCTCAGCTACGAAGT-GAAG-3') (FADS3) derived from the 3'-UTRs of the respective genes were used for filter hybridization at 65°C in 0.5 mM sodium phosphate buffer, pH 7.2; 7% SDS, 1 mM EDTA at 65°C (Church and Gilbert 1984).

[0042] The three genes are ubiquitiously expressed and appear to have similar expression levels in all tissues analyzed. FADS1 revealed a transcript size of 4 0 kb while FADS2 revealed a similar sized transcript of 4.0 kb in addition to a smaller transcript of approximately 3.1 kb. The two FADS2 variants may be due to differential usage of polyadenylation signals (see above). Finally, FADS3 is represented by two transcripts of 1.75 kb and 1.25 kb in size. While the former is in agreement with the usage of the variant polyadenylation signal identified at position 1738 of the cDNA, the small size of the latter transcript can not be explained at present and it does not appear to be due to a differential usage of polyadenylation signals. Possibly, differential splicing and/or exon skipping may be involved in the generation of the variant transcript. However, there is no evidence from cDNA cloning or EST contig assembly to support this possibility.

Comparison with other desaturases

[0043] Local sequence alignments of the deduced amino acid sequences of FADS1, FADS2, and FADS3 with known proteins or protein motifs were done using SwissProt (http://www.ncbi.nlm.nih.gov/cgi-bin/Blast/nph-blast?Jform=0) and the BLASTP and BEAUTY programs at Baylor College of Medicine (http://dot.imgen.bcm.tmc.edu:9331/seq-search/protein-search.html). Amino acid sequence alignments were performed using the CLUSTALW multiple alignment program at http://pbil.ibcp.fr/NPSA/npsa_clustalw.html. Phylogenetic tree assembly was done using the TREECON software Version 1.3b available at http://bioc-www.uia.ac.be/u/yvdp/index.html.

[0044] Overall amino acid identities to known desaturases were found to be in the range of 22% - 27% (Fig. 1). Phylogenetic tree construction revealed a genetic relationship of FADS1, FADS2, and FADS3 to the Δ5-, Δ6- and Δ8-desaturases with some distance to the Δ9-desaturases (Fig. 2). From these analyses it becomes obvious that sequence identity by itself is not a predictor of a specific desaturase activity. For example, Δ5- and Δ6-desaturases from C. elegans demonstrate a higher sequence identity to each other than to the Δ6-desaturases from other species. We therefore conclude that based on simple sequence comparisons it is not feasible to determine the specific functions of FADS1, FADS2, and FADS3. This will be done by transgene expression of the three desaturases combined with gas chromatograpy-mass spectometry.

[0045] Hydropathy plots of FADS1, FADS2 and FADS3 indicate two hydrophiobic sequences predicted to represent transmembrane-spanning domains similar to other desaturases identified thus far (Fig. 1) (reviewed in Sperling et al. 1995).

cDNA amplification of FADS1, FADS2, and FADS3

[0046] The coding sequences of the three genes are amplified in overlapping fragments by performing RT-PCR using oligonucleotide primer pairs derived from the respective cDNA sequences:

(1) FADS1 (Fig. 9 and SEQ ID NOS. 7-12)

[0047] Sense primer TU12-R5 (5'-CGCCTGACAGCCCCTGCT-3') at cDNA position 31-48 in combination with antisense primer TU12-F10 (5'-CAGGTGGCCAATCACAAAAT-3') at cDNA position 671-690 results in a product of 660 bp; sense primer TU12-R7 (5'-CTCAAAGTGGAACCATCTGCTA-3') at cDNA position 645-666 in combination with antisense primer TU12-F9 (5'-GGAAACCCAGTCCATGTTCC-3') at cDNA position 1130-1149 results in a product of 505 bp; sense primer TU12-R6 (5'-CCTGGGCCTTTTCTTCATAGT-3') at cDNA position 1035-1055 in combination with antisense primer TU12-F5 (5'-CTCAAGCTCCCCTCTGCCT-3') at cDNA position 1465-1483 results in a product of 449 bp.

(2) FADS2 (Fig. 9 and SEQ ID NOS. 13-18)

[0048] Sense primer TU13-R4 (5'-TCAGAAGCATAACCTGCGC-3') at cDNA position 98-116 in combination with antisense primer TU13-F7 (5'-CCAGTTCACCAATCAGCAGG-3') at cDNA position 284-303 results in a product of 206 bp; sense primer TU13-R3 (5'-CCCCTGCTGATTGGTGAACT-3') at cDNA position 282-301 in combination with antisense primer TU13-F4 (5'-TGTAGGGCAGGTATTTCAGC -3') at cDNA position 779-798 results in a product of 517 bp; sense primer TU13-R2 (5'-AGCCCATCGAGTACGGCAA-3') at cDNA position 754-772 in combination with antisense primer TU13-F1 (5'-CCTCAGAACAAAAGCCCATC-3') at cDNA position 1416-1435 results in a product of 682 bp.

(3) FADS3 (Fig. 9 and SEQ ID NOS. 19-22)

[0049] Sense primer TU19-R2 (5'-TCTTGCTCGGACCTCGGC-3') at LLCDL3 cDNA position 81-98 in combination with antisense primer TU19-F2 (5'-GTGATCCACACGAACCAGTG-3') at cDNA position 1130-1149 position results in a product of 1069 bp; sens primer TU19-R3 (5'-GAAGAACCCAGCCAGGATG-3') at cDNA position 428-446 in com-

bination with antisense primer TU19-F3 (5'-ACAGCTTTCCCCCAATTCTC-3') at cDNA position 1709-1728 results in a product of 1301 bp.

Short description of Figur s

[0050]

Fig. 1 Comparison of putative amino acid sequences from FADS1, FADS2, FADS3, Borago officinalis, Helianthus annuus and human cytochrome b5. Arrowheads indicate eight invariant amino acid residues typical for the cytochrome b5 domain. Two potential transmembrane domains are boxed. Three histidine motifs $HX_{2(3)}$[XH]H that are conserved within the desaturase family are hatched.
Fig. 2 Phylogenetic tree of fatty acid desaturases.
Fig. 3 (SEQ ID NO. 1) shows the nucleotide sequence of the FADS1 cDNA
Fig. 4 (SEQ ID NO. 2) shows the nucleotide sequence of the FADS2 cDNA
Fig. 5 (SEQ ID NO. 3) shows the nucleotide sequence of the FADS33 cDNA
Fig. 6 (SEQ ID NO. 4) shows the putative amino acid sequence of the predicted FADS1 protein
Fig. 7 (SEQ ID NO. 5) shows the putative amino acid sequence of the predicted FADS2 protein
Fig. 8 (SEQ ID NO. 6) shows the putative amino acid sequence of the predicted FADS3 protein
Fig. 9 (SEQ ID NOS. 7-22) shows the oligonucleotide PCR primers utilized to amplify the FADS1, FADS2, FADS3 cDNA, respectively.

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Annex to the application documents - subsquently filed sequences listing

[0052]

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SEQUENCE LISTING


(1) GENERAL INFORMATION:

     (i) APPLICANT:
          (A) NAME: MultiGen Biotech GmbH
          (B) STREET: Am Hubland
          (C) CITY: Wuerzburg
          (D) STATE: -
          (E) COUNTRY: Germany
          (F) POSTAL CODE (ZIP): 97074
          (G) TELEPHONE: 0931-7058-4340
          (H) TELEFAX: 0931-7058-4355
          (I) TELEX: -

    (ii) TITLE OF INVENTION: cDNA molecules of the members of a gene family
                 encoding human fatty acid desaturases and their use in
                 diagnosis and therapy

   (iii) NUMBER OF SEQUENCES: 22

    (iv) COMPUTER READABLE FORM:
          (A) MEDIUM TYPE: Floppy disk
          (B) COMPUTER: IBM PC compatible
          (C) OPERATING SYSTEM: PC-DOS/MS-DOS
          (D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)


(2) INFORMATION FOR SEQ ID NO: 1:

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          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: protein


    (ix) FEATURE:
          (A) NAME/KEY: Protein
          (B) LOCATION:1..444


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          (A) LENGTH: 4204 base pairs
          (B) TYPE: nucleic acid
          (C) STRANDEDNESS: single
          (D) TOPOLOGY: linear

    (ii) MOLECULE TYPE: DNA (genomic)


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          (B) LOCATION:1..4204
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(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
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(B) LOCATION:1..4089

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

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AGGCTGCCCT GAGGGGCTGG GGAGGGGGTA CCTCATGAGG ACCAGGGTGG AGCTGAGAAG 2640

AGGAGGAGGT GGGGGCTGGA GGTGCTGGTA GCTGAGGGGA CGGGCAAGTG AGAGGGGAGG 2700

GAGGGAAGTC CTGGGAGGAT CCTGAGCTGC TGTTGCAGTC TAACCCACTA ATCAGTTCTT 2760

AGATTCAGGG GAAGGGCAGG CACCAACAAC TCAGAATGGG GGCTTTCGGG GAGGGCGCCT 2820

AGTCCCCCCA GCTCTAAGCA GCCAGGAGGG ACCTGCATCT AAGCATCTGG GTTGCCATGG 2880

CAATGGCATG CCCCCCAGCT ACTGTATGCC CCCGACCCCC GCAGAGGCAG AATGAACCCA 2940

TAGGGAGCTG ATCGTAATGT TTATCATGTT ACTTCCCCAC CCCTACATTT TTTGAAATAA 3000

AATAAGGAAT TTTATTCTCA CTTCCTGTGT TTCCTGCACG CCAATGCCAG GCCATGGTAT 3060

TGGGTGATAG ATGAGGCCCT TCTAGCTGGG CCTGGGCACC AGGAGGGGTC CCCATGCTTG 3120

CATCTCTCTG TATCCCCTCC CTCCCCTGTG GCCATCCCAC CCGCCTCTCC CTGCTGCCTC 3180

TGAAATTCAT TCTGGGGCCC GGAACTTGGT GGAAATGACC CAAAAACATT GGCCCATCTT 3240

CCTCCTCTCA GCAGCCGACC CCAGCCCAAT TCTAAAACAG GGCTGAGAGC CACCTCTCAG 3300

CAGCTGACCC CTACCCAAGG AGGGTGGCAT GGAGGGGCTT GCAGAGACTC TTCCTAACAT 3360

CCTCCCCCCC CAGCTGTCTC CCCAAGTGCA ATCTGCCCTC CCATCCCTGG GCCAGCCAGC 3420

TTCCACAGAG CGCCAGGCCA AACAGAATTC CTGGCCTCCT TGGAAGGGGC TGGAGAAGGC 3480

CGGGAGCAGT GGCTCACGCC TGTAATCCCA GCACTTTGGG AGGCTGAGGC GGGCAGATCA 3540

CAAAGTCAAG AGATTGAGAC CATCCTGGCC AACATGGTGA AACCCCGTCT CTACTAAAAA 3600

TACAAAAATT AGGCCGGGTG CGGTGGCTCA CGCCTGTAAT CCCAGCACTT TGGGAGGCCG 3660

AGGCGGGCAG ATCACGAGGT CAGGAGATCA AGACCATCCT GGCTAACACG GTGAAACCCC 3720

GTCTCTACTA AAAATACAAA AAATTAGCTG GGCGAGGTGG CGGGTGCCTG TAGTCCCAGC 3780

TACGTGGGAG GCTGAGGCAA GAGAATGGCG TGAACCCCGG CGGGGCAGAG CCTGCAGAGA 3840

GCTGAGATCA CACCACTGTA CTCCAGCCTG GGCGACAGCG AGACTCCGTC TCAAAAAAAA 3900

AAAAAAAAAA AATTAGCTGG GCATGGTGGT GCGTGCCTGC AGTCCCAGCT ACTCAGGAGG 3960

CTGAGACGGG AGAATCGCTT GAACCTGGGA GGCAGAGGTT GCAGTGAGCC AAGATCGCTC 4020

ACTCCAGCCT AGCGACAGAG TGAGACTCCA TCTCAAATAA ATAAATAAAT TAATTAATTA 4080

AATTAAATT 4089

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1757 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..1757

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

GGCCGCGGCG GCAGGGCGGG GCCGGAGCAG CGGGCGGCGG CGGAGGCGGC
GCCCGGGAGC 60

GCTCTTCGCT TCCCTCGGGG TCTTGCTCGG ACCTCGGCCA CCGCCTGGGA
TCCCCAGGAC 120

TCGTGCGTGC AGCATGGGCG GCGTCGGGGA GCCGGGACCG CGGGAGGGAC
CCGCGCAGCC 180

GGGGGCACCG CTGCCCACCT TCTGCTGGGA GCAGATCCGC GCGCACGACC
AGCCCGGCGA 240

CAAGTGGCTG GTCATCGAGC GCCGCGTCTA CGACATCAGC CGCTGGGCAC
AGCGGCACCC 300

AGGGGGCAGC CGCCTCATCG GCCACCACGG CGCTGAGGAC GCCACGGATG
CCTTCCGTGC 360

CTTCCATCAA GATCTCAATT TTGTGCGCAA GTTCCTACAG CCCCTGTTGA
TTGGAGAGCT 420

GGCTCCGGAA GAACCCAGCC AGGATGGACC CCTGAATGCG CAGCTGGTCG
AGGACTTCCG 480

AGCCCTGCAC CAGGCAGCCG AGGACATGAA GCTGTTTGAT GCCAGTCCCA
CCTTCTTTGC 540

TTTCCTACTG GGCCACATCC TGGCCATGGA GGTGCTGGCC TGGCTCCTTA
TCTACCTCCT 600

GGGTCCTGGC TGGGTGCCCA GTGCCCTGGC CGCCTTCATC CTGGCCATCT
CTCAGGCTCA 660

GTCCTGGTGT CTGCAGCATG ACCTGGGCCA TGCCTCCATC TTCAAGAAGT
CCTGGTGGAA 720

CCACGTGGCC CAGAAGTTCG TGATGGGGCA GCTAAAGGGC TTCTCCGCCC
ACTGGTGGAA 780

CTTCCGCCAC TTCCAGCACC ACGCCAAGCC CAACATCTTC CACAAAGACC
CAGACGTGAC 840

GGTGGCGCCC GTCTTCCTCC TGGGGGAGTC ATCCGTCGAG TATGGCAAGA
AGAAACGCAG 900

ATACCTACCC TACAACCAGC AGCACCTGTA CTTCTTCCTG ATCGGCCCGC
CGCTGCTCAC 960

CCTGGTGAAC TTTGAAGTGG AAAATCTGGC GTACATGCTG GTGTGCATGC
AGTGGGCGGA 1020

TTTGCTCTGG GCCGCCAGCT TCTATGCCCG CTTCTTCTTA TCCTACCTCC
CCTTCTACGG 1080

CGTCCCTGGG GTGCTGCTCT TCTTTGTTGC TGTCAGGGTC CTGGAAAGCC
ACTGGTTCGT 1140

GTGGATCACA CAGATGAACC ACATCCCCAA GGAGATCGGC CACGAGAAGC
ACCGGGACTG 1200

GGTCAGCTCT CAGCTGGCAG CCACCTGCAA CGTGGAGCCC TCACTTTTCA
CCAACTGGTT 1260

CAGCGGGCAC CTCAACTTCC AGATCGAGCA CCACCTCTTC CCCAGGATGC
CGAGACACAA 1320

CTACAGCCGG GTGGCCCCGC TGGTCAAGTC GCTGTGTGCC AAGCACGGCC
TCAGCTACGA 1380

AGTGAAGCCC TTCCTCACCG CGCTGGTGGA CATCGTCAGG TCCCTGAAGA
AGTCTGGTGA 1440

CATCTGGCTG GACGCCTACC TCCATCAGTG AAGGCAACAC CCAGGCGGGC
AGAGAAGGGC 1500

TCAGGGCACC AGCAACCAAG CCAGCCCCGG CGGGATCGAT ACCCCCACCC
CTCCACTGGC 1560

CAGCCTGGGG GTGCCCTGCC TGCCCTCCTG GTACTGTTGT CTTCCCCTCG
GCCCCCTCAC 1620

ATGTGTATTC AGCAGCCCTA TGGCCTTGGC TCTGGGCCTG ATGGGACAGG
GGTAGAGGGA 1680

AGGTGAGCAT AGCACATTTT CCTAGAGCGA GAATTGGGGG AAAGCTGTTA
TTTTTATATT 1740

AAAATACATT CAGATGT 1757

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 444 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION:1..444

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

```
Met Ala Pro Asp Pro Val Ala Ala Glu Thr Ala Ala Gln Gly Pro Thr
1               5                   10                  15

Pro Arg Tyr Phe Thr Trp Asp Glu Val Ala Gln Arg Ser Gly Cys Glu
            20                  25                  30

Glu Arg Trp Leu Val Ile Asp Arg Lys Val Tyr Asn Ile Ser Glu Phe
        35                  40                  45

Thr Arg Arg His Pro Gly Gly Ser Arg Val Ile Ser His Tyr Ala Gly
    50                  55                  60

Gln Asp Ala Thr Asp Pro Phe Val Ala Phe His Ile Asn Lys Gly Leu
65                  70                  75                  80

Val Lys Lys Tyr Met Asn Ser Leu Leu Ile Gly Glu Leu Ser Pro Glu
                85                  90                  95

Gln Pro Ser Phe Glu Pro Thr Lys Asn Lys Glu Leu Thr Asp Glu Phe
            100                 105                 110

Arg Glu Leu Arg Ala Thr Val Glu Arg Met Gly Leu Met Lys Ala Asn
        115                 120                 125

His Val Phe Phe Leu Leu Tyr Leu Leu His Ile Leu Leu Leu Asp Gly
    130                 135                 140

Ala Ala Trp Leu Thr Leu Trp Val Phe Gly Thr Ser Phe Leu Pro Phe
145                 150                 155                 160

Leu Leu Cys Ala Val Leu Leu Ser Ala Val Gln Ala Gln Ala Gly Trp
                165                 170                 175

Leu Gln His Asp Phe Gly His Leu Ser Val Phe Ser Thr Ser Lys Trp
            180                 185                 190

Asn His Leu Leu His His Phe Val Ile Gly His Leu Lys Gly Ala Pro
        195                 200                 205

Ala Ser Trp Trp Asn His Met His Phe Gln His His Ala Lys Pro Asn
    210                 215                 220

Cys Phe Arg Lys Asp Pro Asp Ile Asn Met His Pro Phe Phe Phe Ala
225                 230                 235                 240
```

```
Leu Gly Lys Ile Leu Ser Val Glu Leu Gly Lys Gln Lys Lys Lys Tyr
                245                 250                 255

Met Pro Tyr Asn His Gln His Lys Tyr Phe Phe Leu Ile Gly Pro Pro
            260                 265                 270

Ala Leu Leu Pro Leu Tyr Phe Gln Trp Tyr Ile Phe Tyr Phe Val Ile
        275                 280                 285

Gln Arg Lys Lys Trp Val Asp Leu Ala Trp Met Ile Thr Phe Tyr Val
    290                 295                 300

Arg Phe Phe Leu Thr Tyr Val Pro Leu Leu Gly Leu Lys Ala Phe Leu
305                 310                 315                 320

Gly Leu Phe Phe Ile Val Arg Phe Leu Glu Ser Asn Trp Phe Val Trp
                325                 330                 335

Val Thr Gln Met Asn His Ile Pro Met His Ile Asp His Asp Arg Asn
            340                 345                 350

Met Asp Trp Val Ser Thr Gln Leu Gln Ala Thr Cys Asn Val His Lys
        355                 360                 365

Ser Ala Phe Asn Asp Trp Phe Ser Gly His Leu Asn Phe Gln Ile Glu
    370                 375                 380

His His Leu Phe Pro Thr Met Pro Arg His Asn Tyr His Lys Val Ala
385                 390                 395                 400

Pro Leu Val Gln Ser Leu Cys Ala Lys His Gly Ile Glu Tyr Gln Ser
                405                 410                 415

Lys Pro Leu Leu Ser Ala Phe Ala Asp Ile Ile His Ser Leu Lys Glu
            420                 425                 430

Ser Gly Gln Leu Trp Leu Asp Ala Tyr Leu His Gln
        435                 440
```

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 444 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION:1..444

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

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Met Gly Lys Gly Gly Asn Gln Gly Glu Gly Ala Ala Glu Arg Glu Val
1               5                   10                  15

Ser Val Pro Thr Phe Ser Trp Glu Glu Ile Gln Lys His Asn Leu Arg
            20                  25                  30

Thr Asp Arg Trp Leu Val Ile Asp Arg Lys Val Tyr Asn Ile Thr Lys
        35                  40                  45

Trp Ser Ile Gln His Pro Gly Gly Gln Arg Val Ile Gly His Tyr Ala
    50                  55                  60

Gly Glu Asp Ala Thr Asp Ala Phe Arg Ala Phe His Pro Asp Leu Glu
65                  70                  75                  80

Phe Val Gly Lys Phe Leu Lys Pro Leu Leu Ile Gly Glu Leu Ala Pro
                85                  90                  95

Glu Glu Pro Ser Gln Asp His Gly Lys Asn Ser Lys Ile Thr Glu Asp
            100                 105                 110

Phe Arg Ala Leu Arg Lys Thr Ala Glu Asp Met Asn Leu Phe Lys Thr
        115                 120                 125

Asn His Val Phe Phe Leu Leu Leu Leu Ala His Ile Ile Ala Leu Glu
    130                 135                 140

Ser Ile Ala Trp Phe Thr Val Phe Tyr Phe Gly Asn Gly Trp Ile Pro
145                 150                 155                 160

Thr Leu Ile Thr Ala Phe Val Leu Ala Thr Ser Gln Ala Gln Ala Gly
                165                 170                 175

Trp Leu Gln His Asp Tyr Gly His Leu Ser Val Tyr Arg Lys Pro Lys
            180                 185                 190

Trp Asn His Leu Val His Lys Phe Val Ile Gly His Leu Lys Gly Ala
        195                 200                 205

Ser Ala Asn Trp Trp Asn His Arg His Phe Gln His His Ala Lys Pro
    210                 215                 220

Asn Ile Phe His Lys Asp Pro Asp Val Asn Met Leu His Val Phe Val
225                 230                 235                 240
```

Leu Gly Glu Trp Gln Pro Ile Glu Tyr Gly Lys Lys Lys Leu Lys Tyr
245 250 255

Leu Pro Tyr Asn His Gln His Glu Tyr Phe Phe Leu Ile Gly Pro Pro
260 265 270

Leu Leu Ile Pro Met Tyr Phe Gln Tyr Gln Ile Ile Met Thr Met Ile
275 280 285

Val His Lys Asn Trp Val Asp Leu Ala Trp Ala Val Ser Tyr Tyr Ile
290 295 300

Arg Phe Phe Ile Thr Tyr Ile Pro Phe Tyr Gly Ile Leu Gly Ala Leu
305 310 315 320

Leu Phe Leu Asn Phe Ile Arg Phe Leu Glu Ser His Trp Phe Val Trp
325 330 335

Val Thr Gln Met Asn His Ile Val Met Glu Ile Asp Gln Glu Ala Tyr
340 345 350

Arg Asp Trp Phe Ser Ser Gln Leu Thr Ala Thr Cys Asn Val Glu Gln
355 360 365

Ser Phe Phe Asn Asp Trp Phe Ser Gly His Leu Asn Phe Gln Ile Glu
370 375 380

His His Leu Phe Pro Thr Met Pro Arg His Asn Leu His Lys Ile Ala
385 390 395 400

Pro Leu Val Lys Ser Leu Cys Ala Lys His Gly Ile Glu Tyr Gln Glu
405 410 415

Lys Pro Leu Leu Arg Ala Leu Leu Asp Ile Ile Arg Ser Leu Lys Lys
420 425 430

Ser Gly Lys Leu Trp Leu Asp Ala Tyr Leu His Lys
435 440

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 445 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(ix) FEATURE:
(A) NAME/KEY: Protein
(B) LOCATION:1..445

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

```
Met Gly Gly Val Gly Glu Pro Gly Pro Arg Glu Gly Pro Ala Gln Pro
1               5                   10                  15

Gly Ala Pro Leu Pro Thr Phe Cys Trp Glu Gln Ile Arg Ala His Asp
            20                  25                  30

Gln Pro Gly Asp Lys Trp Leu Val Ile Glu Arg Arg Val Tyr Asp Ile
        35                  40                  45

Ser Arg Trp Ala Gln Arg His Pro Gly Gly Ser Arg Leu Ile Gly His
    50                  55                  60

His Gly Ala Glu Asp Ala Thr Asp Ala Phe Arg Ala Phe His Gln Asp
65                  70                  75                  80

Leu Asn Phe Val Arg Lys Phe Leu Gln Pro Leu Leu Ile Gly Glu Leu
                85                  90                  95

Ala Pro Glu Glu Pro Ser Gln Asp Gly Pro Leu Asn Ala Gln Leu Val
            100                 105                 110

Glu Asp Phe Arg Ala Leu His Gln Ala Ala Glu Asp Met Lys Leu Phe
        115                 120                 125

Asp Ala Ser Pro Thr Phe Phe Ala Phe Leu Leu Gly His Ile Leu Ala
    130                 135                 140

Met Glu Val Leu Ala Trp Leu Leu Ile Tyr Leu Leu Gly Pro Gly Trp
145                 150                 155                 160

Val Pro Ser Ala Leu Ala Ala Phe Ile Leu Ala Ile Ser Gln Ala Gln
                165                 170                 175

Ser Trp Cys Leu Gln His Asp Leu Gly His Ala Ser Ile Phe Lys Lys
            180                 185                 190

Ser Trp Trp Asn His Val Ala Gln Lys Phe Val Met Gly Gln Leu Lys
        195                 200                 205

Gly Phe Ser Ala His Trp Trp Asn Phe Arg His Phe Gln His His Ala
    210                 215                 220

Lys Pro Asn Ile Phe His Lys Asp Pro Asp Val Thr Val Ala Pro Val
225                 230                 235                 240
```

Phe Leu Leu Gly Glu Ser Ser Val Glu Tyr Gly Lys Lys Lys Arg Arg
245 250 255

Tyr Leu Pro Tyr Asn Gln Gln His Leu Tyr Phe Phe Leu Ile Gly Pro
260 265 270

Pro Leu Leu Thr Leu Val Asn Phe Glu Val Glu Asn Leu Ala Tyr Met
275 280 285

Leu Val Cys Met Gln Trp Ala Asp Leu Leu Trp Ala Ala Ser Phe Tyr
290 295 300

Ala Arg Phe Phe Leu Ser Tyr Leu Pro Phe Tyr Gly Val Pro Gly Val
305 310 315 320

Leu Leu Phe Phe Val Ala Val Arg Val Leu Glu Ser His Trp Phe Val
325 330 335

Trp Ile Thr Gln Met Asn His Ile Pro Lys Glu Ile Gly His Glu Lys
340 345 350

His Arg Asp Trp Val Ser Ser Gln Leu Ala Ala Thr Cys Asn Val Glu
355 360 365

Pro Ser Leu Phe Thr Asn Trp Phe Ser Gly His Leu Asn Phe Gln Ile
370 375 380

Glu His His Leu Phe Pro Arg Met Pro Arg His Asn Tyr Ser Arg Val
385 390 395 400

Ala Pro Leu Val Lys Ser Leu Cys Ala Lys His Gly Leu Ser Tyr Glu
405 410 415

Val Lys Pro Phe Leu Thr Ala Leu Val Asp Ile Val Arg Ser Leu Lys
420 425 430

Lys Ser Gly Asp Ile Trp Leu Asp Ala Tyr Leu His Gln
435 440 445

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..18

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

TCGTCCCCGA CAGTCCGC 18

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

TAAAACACTA ACCGGTGGAC 20

(2) INFORMATION FOR SEQ ID NO: 9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..22

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

ATCGTCTACC AAGGTGAAAC TC 22

(2) INFORMATION FOR SEQ ID NO: 10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:

CCTTGTACCT GACCCAAAGG 20

(2) INFORMATION FOR SEQ ID NO: 11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..21

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:

TGATACTTCT TTTCCGGGTC C 21

(2) INFORMATION FOR SEQ ID NO: 12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..19

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

TCCGTCTCCC CTCGAACTC 19

(2) INFORMATION FOR SEQ ID NO: 13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..19

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

CGCGTCCAAT ACGAAGACT 19

(2) INFORMATION FOR SEQ ID NO: 14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

GGACGACTAA CCACTTGACC 20

(2) INFORMATION FOR SEQ ID NO: 15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

TCAAGTGGTT AGTCGTCCCC 20

(2) INFORMATION FOR SEQ ID NO: 16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:

CGACTTTATG GACGGGATGT 20

(2) INFORMATION FOR SEQ ID NO: 17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..19

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

AACGGCATGA GCTACCCGA 19

(2) INFORMATION FOR SEQ ID NO: 18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18:

CTACCCGAAA ACAAGACTCC 20

(2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 18 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..18

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 19:

CGGCTCCAGG CTCGTTCT 18

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:

GTGACCAAGC ACACCTAGTG 20

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..19

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

GTAGGACCGA CCCAAGAAG 19

(2) INFORMATION FOR SEQ ID NO: 22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: exon
(B) LOCATION:1..20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

CTCTTAACCC CCTTTCGACA 20

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<120> cDNA molecules of the members of gene family encoding human fatty acid desaturases and their use in diagnosis and therapy

<130> MultiGene Anm. 99/002 EP

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<210> 2
<211> 4089
<212> DNA
<213> Unknown Organism

<220>
<223> Description of Unknown Organism:

unknown

<400> 2
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<210> 3
<211> 1757
<212> DNA
<213> Unknown Organism

<220>
<223> Description of Unknown Organism:

unknown

<400> 3
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<210> 4
<211> 444
<212> PRT
<213> Unknown Organism

<220>
<223> Description of Unknown Organism:

unknown

<400> 4
Met Ala Pro Asp Pro Val Ala Ala Glu Thr Ala Ala Gln Gly Pro Thr
1 5 10 15

Pro Arg Tyr Phe Thr Trp Asp Glu Val Ala Gln Arg Ser Gly Cys Glu
20 25 30

Glu Arg Trp Leu Val Ile Asp Arg Lys Val Tyr Asn Ile Ser Glu Phe
35 40 45

Thr Arg Arg His Pro Gly Gly Ser Arg Val Ile Ser His Tyr Ala Gly
50 55 60

Gln Asp Ala Thr Asp Pro Phe Val Ala Phe His Ile Asn Lys Gly Leu
65 70 75 80

Val Lys Lys Tyr Met Asn Ser Leu Leu Ile Gly Glu Leu Ser Pro Glu
85 90 95

Gln Pro Ser Phe Glu Pro Thr Lys Asn Lys Glu Leu Thr Asp Glu Phe
100 105 110

Arg Glu Leu Arg Ala Thr Val Glu Arg Met Gly Leu Met Lys Ala Asn
115 120 125

His Val Phe Phe Leu Leu Tyr Leu Leu His Ile Leu Leu Leu Asp Gly
130 135 140

Ala Ala Trp Leu Thr Leu Trp Val Phe Gly Thr Ser Phe Leu Pro Phe
145 150 155 160

Leu Leu Cys Ala Val Leu Leu Ser Ala Val Gln Ala Gln Ala Gly Trp
165 170 175

Leu Gln His Asp Phe Gly His Leu Ser Val Phe Ser Thr Ser Lys Trp
180 185 190

Asn His Leu Leu His His Phe Val Ile Gly His Leu Lys Gly Ala Pro
195 200 205

Ala Ser Trp Trp Asn His Met His Phe Gln His His Ala Lys Pro Asn
210 215 220

Cys Phe Arg Lys Asp Pro Asp Ile Asn Met His Pro Phe Phe Phe Ala
225 230 235 240

Leu Gly Lys Ile Leu Ser Val Glu Leu Gly Lys Gln Lys Lys Lys Tyr
245 250 255

Met Pro Tyr Asn His Gln His Lys Tyr Phe Phe Leu Ile Gly Pro Pro
260 265 270

Ala Leu Leu Pro Leu Tyr Phe Gln Trp Tyr Ile Phe Tyr Phe Val Ile
275 280 285

Gln Arg Lys Lys Trp Val Asp Leu Ala Trp Met Ile Thr Phe Tyr Val
290 295 300

Arg Phe Phe Leu Thr Tyr Val Pro Leu Leu Gly Leu Lys Ala Phe Leu
305 310 315 320

Gly Leu Phe Phe Ile Val Arg Phe Leu Glu Ser Asn Trp Phe Val Trp
325 330 335

Val Thr Gln Met Asn His Ile Pro Met His Ile Asp His Asp Arg Asn
340 345 350

Met Asp Trp Val Ser Thr Gln Leu Gln Ala Thr Cys Asn Val His Lys
355 360 365

Ser Ala Phe Asn Asp Trp Phe Ser Gly His Leu Asn Phe Gln Ile Glu
370 375 380

His His Leu Phe Pro Thr Met Pro Arg His Asn Tyr His Lys Val Ala
385 390 395 400

Pro Leu Val Gln Ser Leu Cys Ala Lys His Gly Ile Glu Tyr Gln Ser
405 410 415

Lys Pro Leu Leu Ser Ala Phe Ala Asp Ile Ile His Ser Leu Lys Glu
420 425 430

Ser Gly Gln Leu Trp Leu Asp Ala Tyr Leu His Gln
435 440

<210> 5
<211> 444
<212> PRT
<213> Unknown Organism

<220>
<223> Description of Unknown Organism:

unknown

<400> 5
Met Gly Lys Gly Gly Asn Gln Gly Glu Gly Ala Ala Glu Arg Glu Val
1 5 10 15

Ser Val Pro Thr Phe Ser Trp Glu Glu Ile Gln Lys His Asn Leu Arg
20 25 30

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Thr Asp Arg Trp Leu Val Ile Asp Arg Lys Val Tyr Asn Ile Thr Lys
            35                  40                  45

Trp Ser Ile Gln His Pro Gly Gly Gln Arg Val Ile Gly His Tyr Ala
        50                  55                  60

Gly Glu Asp Ala Thr Asp Ala Phe Arg Ala Phe His Pro Asp Leu Glu
65                  70                  75                  80

Phe Val Gly Lys Phe Leu Lys Pro Leu Leu Ile Gly Glu Leu Ala Pro
                85                  90                  95

Glu Glu Pro Ser Gln Asp His Gly Lys Asn Ser Lys Ile Thr Glu Asp
            100                 105                 110

Phe Arg Ala Leu Arg Lys Thr Ala Glu Asp Met Asn Leu Phe Lys Thr
        115                 120                 125

Asn His Val Phe Phe Leu Leu Leu Leu Ala His Ile Ile Ala Leu Glu
    130                 135                 140

Ser Ile Ala Trp Phe Thr Val Phe Tyr Phe Gly Asn Gly Trp Ile Pro
145                 150                 155                 160

Thr Leu Ile Thr Ala Phe Val Leu Ala Thr Ser Gln Ala Gln Ala Gly
                165                 170                 175

Trp Leu Gln His Asp Tyr Gly His Leu Ser Val Tyr Arg Lys Pro Lys
            180                 185                 190

Trp Asn His Leu Val His Lys Phe Val Ile Gly His Leu Lys Gly Ala
        195                 200                 205

Ser Ala Asn Trp Trp Asn His Arg His Phe Gln His His Ala Lys Pro
    210                 215                 220

Asn Ile Phe His Lys Asp Pro Asp Val Asn Met Leu His Val Phe Val
225                 230                 235                 240

Leu Gly Glu Trp Gln Pro Ile Glu Tyr Gly Lys Lys Lys Leu Lys Tyr
                245                 250                 255
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Leu Pro Tyr Asn His Gln His Glu Tyr Phe Phe Leu Ile Gly Pro Pro
260 265 270

Leu Leu Ile Pro Met Tyr Phe Gln Tyr Gln Ile Ile Met Thr Met Ile
275 280 285

Val His Lys Asn Trp Val Asp Leu Ala Trp Ala Val Ser Tyr Tyr Ile
290 295 300

Arg Phe Phe Ile Thr Tyr Ile Pro Phe Tyr Gly Ile Leu Gly Ala Leu
305 310 315 320

Leu Phe Leu Asn Phe Ile Arg Phe Leu Glu Ser His Trp Phe Val Trp
325 330 335

Val Thr Gln Met Asn His Ile Val Met Glu Ile Asp Gln Glu Ala Tyr
340 345 350

Arg Asp Trp Phe Ser Ser Gln Leu Thr Ala Thr Cys Asn Val Glu Gln
355 360 365

Ser Phe Phe Asn Asp Trp Phe Ser Gly His Leu Asn Phe Gln Ile Glu
370 375 380

His His Leu Phe Pro Thr Met Pro Arg His Asn Leu His Lys Ile Ala
385 390 395 400

Pro Leu Val Lys Ser Leu Cys Ala Lys His Gly Ile Glu Tyr Gln Glu
405 410 415

Lys Pro Leu Leu Arg Ala Leu Leu Asp Ile Ile Arg Ser Leu Lys Lys
420 425 430

Ser Gly Lys Leu Trp Leu Asp Ala Tyr Leu His Lys
435 440

<210> 6
<211> 445
<212> PRT
<213> Unknown Organism

<220>
<223> Description of Unknown Organism:

unknown

<400> 6

Met Gly Gly Val Gly Glu Pro Gly Pro Arg Glu Gly Pro Ala Gln Pro
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Gly Ala Pro Leu Pro Thr Phe Cys Trp Glu Gln Ile Arg Ala His Asp
20 25 30

Gln Pro Gly Asp Lys Trp Leu Val Ile Glu Arg Arg Val Tyr Asp Ile
35 40 45

Ser Arg Trp Ala Gln Arg His Pro Gly Gly Ser Arg Leu Ile Gly His
50 55 60

His Gly Ala Glu Asp Ala Thr Asp Ala Phe Arg Ala Phe His Gln Asp
65 70 75 80

Leu Asn Phe Val Arg Lys Phe Leu Gln Pro Leu Leu Ile Gly Glu Leu
85 90 95

Ala Pro Glu Glu Pro Ser Gln Asp Gly Pro Leu Asn Ala Gln Leu Val
100 105 110

Glu Asp Phe Arg Ala Leu His Gln Ala Ala Glu Asp Met Lys Leu Phe
115 120 125

Asp Ala Ser Pro Thr Phe Phe Ala Phe Leu Leu Gly His Ile Leu Ala
130 135 140

Met Glu Val Leu Ala Trp Leu Leu Ile Tyr Leu Leu Gly Pro Gly Trp
145 150 155 160

Val Pro Ser Ala Leu Ala Ala Phe Ile Leu Ala Ile Ser Gln Ala Gln
165 170 175

Ser Trp Cys Leu Gln His Asp Leu Gly His Ala Ser Ile Phe Lys Lys
180 185 190

Ser Trp Trp Asn His Val Ala Gln Lys Phe Val Met Gly Gln Leu Lys
195 200 205

Gly Phe Ser Ala His Trp Trp Asn Phe Arg His Phe Gln His His Ala
210 215 220

Lys Pro Asn Ile Phe His Lys Asp Pro Asp Val Thr Val Ala Pro Val
225 230 235 240

Phe Leu Leu Gly Glu Ser Ser Val Glu Tyr Gly Lys Lys Lys Arg Arg
245 250 255

Tyr Leu Pro Tyr Asn Gln Gln His Leu Tyr Phe Phe Leu Ile Gly Pro
260 265 270

Pro Leu Leu Thr Leu Val Asn Phe Glu Val Glu Asn Leu Ala Tyr Met
275 280 285

Leu Val Cys Met Gln Trp Ala Asp Leu Leu Trp Ala Ala Ser Phe Tyr
290 295 300

Ala Arg Phe Phe Leu Ser Tyr Leu Pro Phe Tyr Gly Val Pro Gly Val
305 310 315 320

Leu Leu Phe Phe Val Ala Val Arg Val Leu Glu Ser His Trp Phe Val
325 330 335

Trp Ile Thr Gln Met Asn His Ile Pro Lys Glu Ile Gly His Glu Lys
340 345 350

His Arg Asp Trp Val Ser Ser Gln Leu Ala Ala Thr Cys Asn Val Glu
355 360 365

Pro Ser Leu Phe Thr Asn Trp Phe Ser Gly His Leu Asn Phe Gln Ile
370 375 380

Glu His His Leu Phe Pro Arg Met Pro Arg His Asn Tyr Ser Arg Val
385 390 395 400

Ala Pro Leu Val Lys Ser Leu Cys Ala Lys His Gly Leu Ser Tyr Glu
405 410 415

Val Lys Pro Phe Leu Thr Ala Leu Val Asp Ile Val Arg Ser Leu Lys
420 425 430

Lys Ser Gly Asp Ile Trp Leu Asp Ala Tyr Leu His Gln
435 440 445

<210> 7
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Claims

1. An isolated cDNA molecule selected from the group consisting of

   (a) a polynucleotide having at least a 65 % homology, preferably at least a 80 % homology with a polynucleotide encoding a polypeptide selected from the group consisting of the polypeptides of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6;
   (b) a polynucleotide having at least a 65 % homology, preferably at least a 80 % homology with a polynucleotide which by virtue of the redundancy of the genetic code, encodes the same polypeptide selected from the group consisting of the polypeptides of SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6;
   (c) a DNA molecule capable of hybridization under stringent conditions to a DNA molecule according to (a) or (b);
   (d) a polynucleotide which is complementary to the polynucleotide of (a), (b) or (c); and
   (e) a oligonucleotide comprising at least 15 consecutive nucleotides of the polynucleotide of (a), (b), (c) or (d).

2. An isolated cDNA molecule selected from the group consisting of

   (a) a polynucleotide having at least a 65 % homology, preferably at least a 80 % homology with a polynucleotide sequence selected from the group consisting of the polynucleotides of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3;
   (b) a DNA molecule capable of hybridization under stringent conditions to a DNA molecule according to (a);
   (c) a polynucleotide which is complementary to the polynucleotide of (a) or (b);
   (d) a oligonucleotide comprising at least 15 consecutive nucleotides of the polynucleotide of (a), (b) or (c); and
   (e) a DNA which is synonymous to the DNAs of (a), (b), (c) or (d) due to the degeneracy of the genetic code.

3. A DNA comprising a nucleotide sequence with at least a 65 % homology with the nucleotide sequences as defined in claim 1 or 2.

4. A recombinant vector comprising the DNA as claimed in any of claims 1 to 3.

5. A transgenic host cell comprising the DNA as claimed in any of claims 1 to 3.

6. A transgenetic host cell transformed by the DNA according to any of claims 1 to 3 or the vector according to claim 4, a corresponding transgenetic organism or a corresponding transgenetic knock-in or knock-out animal model.

7. A polypeptide comprising at least 65 % of a polypeptide sequence selected from the group consisting of the polypeptides of SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, or its salt.

8. A polypeptide comprising a polypeptide sequence with at least a 85 % homology with the polypeptide sequence as claimed in claim 7, or its salt.

9. A peptide comprising at least 15 consecutive amino acids of the polypeptide as claimed in claim 7, or its salt.

10. A polypeptide having substantially the same amino acid sequence as the polypeptide as claimed in claim 7, or having a variant of the amino acid sequence of the polypeptide as claimed in claim 7 with a deletion, addition or substitution of 1 to 10 amino acids, or its salt.

11. A process for producing a polypeptide comprising expressing from the host cell of claim 5 or 6 a polypeptide encoded by the DNA as claimed in any of claims 1 to 3.

12. An antibody against the polypeptide of any of claims 7 to 10.

13. A oligonucleotide primer having a nucleotide sequence selected from the group consisting of the nucleotide sequences of SEQ ID NO: 7 to SEQ ID NO: 22.

14. A method of screening for modulators in known assays using constructs or of screening for interacting proteins or factors using state of the art technologies.

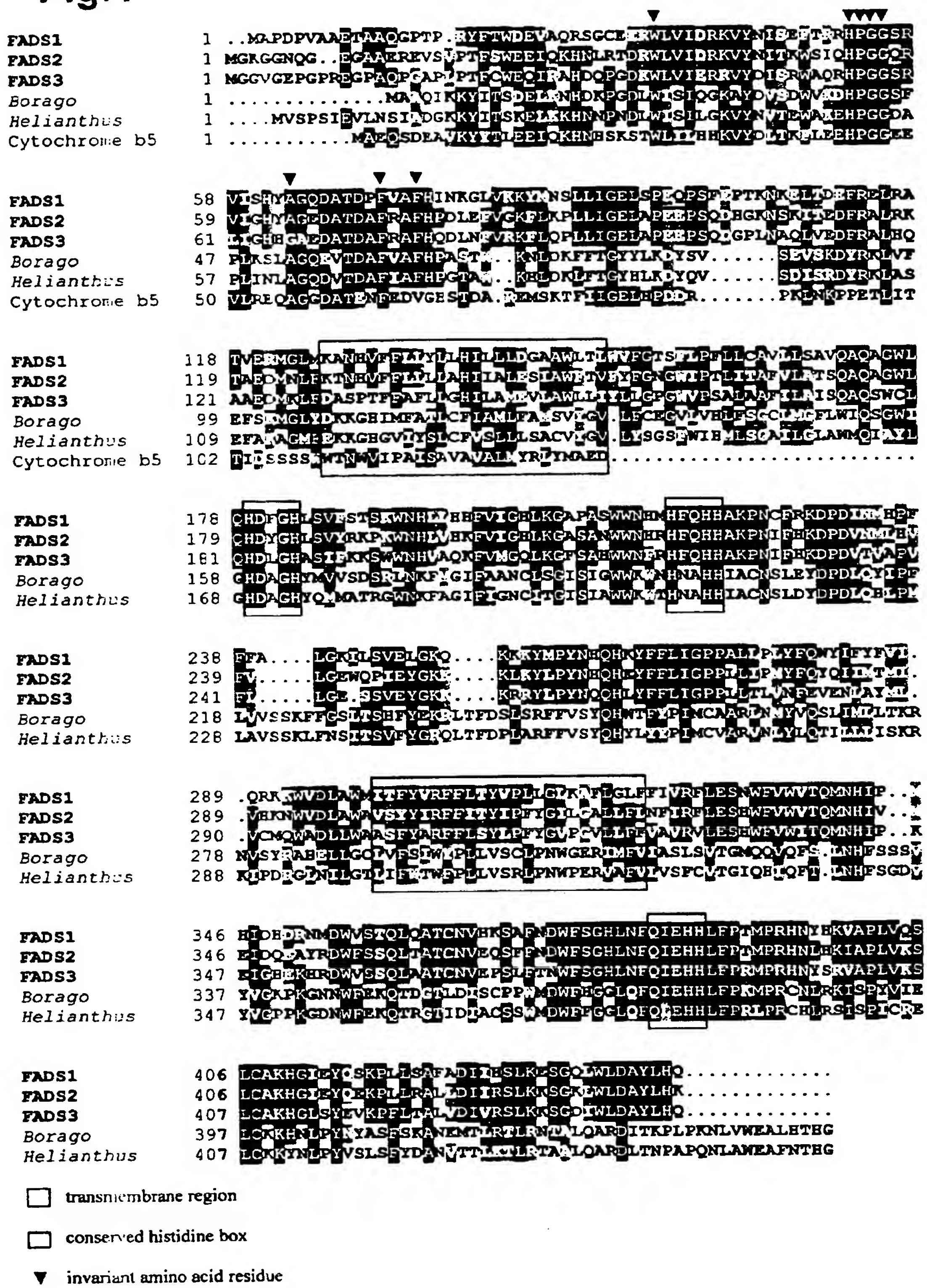
15. A method of screening chemical libraries comprising transformed cell lines.

16. A compound which alters or reacts with at least one epitope of the proteins and which is obtained by screening methods as claimed in claim 14 or 15.

17. The use of the antibodies according to claim 12 for diagnostic or therapeutic purposes.

18. A pharmaceutical composition comprising as an effective component an effective amount of the peptide as claimed in any of claims 7 to 10, or its salt, and a pharmaceutically acceptable carrier or diluent.

Fig.1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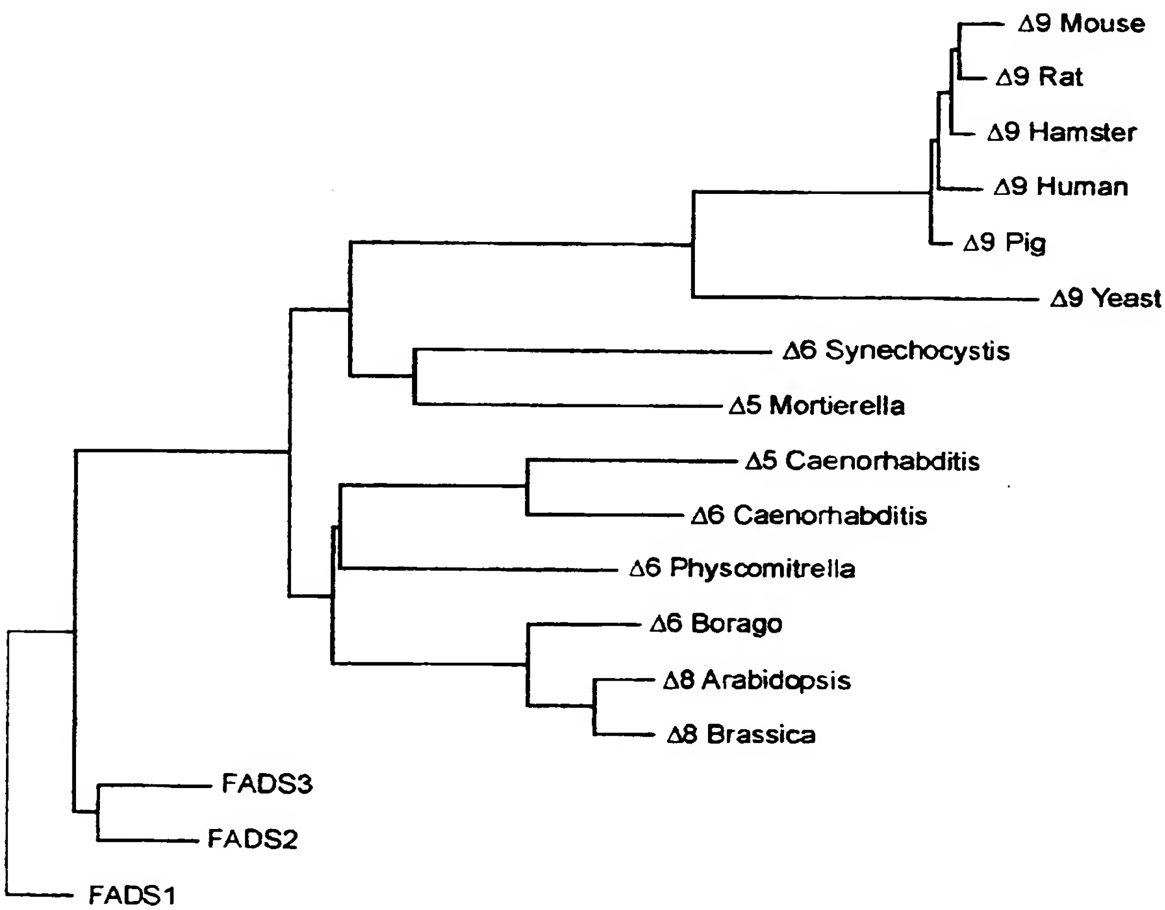
FADS2
FADS3
Borago
Helianthus
Cytochrome b5
transmembrane region
conserved histidine box
invariant amino acid residue

Fig.2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Δ9 Human
Δ9 Pig
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Δ6 Synechocystis
Δ5 Mortierella
Δ5 Caenorhabditis
Δ6 Caenorhabditis
Δ6 Physcomitrella
Δ6 Borago
Δ8 Arabidopsis
Δ8 Brassica
FADS3
FADS2
FADS1

Fig. 3

FADS1 cDNA

CACTCCTGGAGCCCGCGGACCCCGAGCACGCGCCTGACAGCCCCTGCTGGCCCGGCGCGCGGCG
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Fig. 3 cont.

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Fig. 4

FADS2 cDNA

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Fig. 4 cont.

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Fig. 5

FADS3 cDNA

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Fig. 6

FADS1

Met Ala Pro Asp Pro Val Ala Ala Glu Thr Ala Ala Gln Gly Pro Thr
1 5 10 15

Pro Arg Tyr Phe Thr Trp Asp Glu Val Ala Gln Arg Ser Gly Cys Glu
20 25 30

Glu Arg Trp Leu Val Ile Asp Arg Lys Val Tyr Asn Ile Ser Glu Phe
35 40 45

Thr Arg Arg His Pro Gly Gly Ser Arg Val Ile Ser His Tyr Ala Gly
50 55 60

Gln Asp Ala Thr Asp Pro Phe Val Ala Phe His Ile Asn Lys Gly Leu
65 70 75 80

Val Lys Lys Tyr Met Asn Ser Leu Leu Ile Gly Glu Leu Ser Pro Glu
85 90 95

Gln Pro Ser Phe Glu Pro Thr Lys Asn Lys Glu Leu Thr Asp Glu Phe
100 105 110

Arg Glu Leu Arg Ala Thr Val Glu Arg Met Gly Leu Met Lys Ala Asn
115 120 125

His Val Phe Phe Leu Leu Tyr Leu Leu His Ile Leu Leu Leu Asp Gly
130 135 140

Ala Ala Trp Leu Thr Leu Trp Val Phe Gly Thr Ser Phe Leu Pro Phe
145 150 155 160

Leu Leu Cys Ala Val Leu Leu Ser Ala Val Gln Ala Gln Ala Gly Trp
165 170 175

Leu Gln His Asp Phe Gly His Leu Ser Val Phe Ser Thr Ser Lys Trp
180 185 190

Asn His Leu Leu His His Phe Val Ile Gly His Leu Lys Gly Ala Pro
195 200 205

Ala Ser Trp Trp Asn His Met His Phe Gln His His Ala Lys Pro Asn
210 215 220

Cys Phe Arg Lys Asp Pro Asp Ile Asn Met His Pro Phe Phe Phe Ala
225 230 235 240

Leu Gly Lys Ile Leu Ser Val Glu Leu Gly Lys Gln Lys Lys Lys Tyr
245 250 255

Met Pro Tyr Asn His Gln His Lys Tyr Phe Phe Leu Ile Gly Pro Pro
260 265 270

Ala Leu Leu Pro Leu Tyr Phe Gln Trp Tyr Ile Phe Tyr Phe Val Ile
275 280 285

Fig. 6 cont.

```
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305                 310                 315                 320
Gly Leu Phe Phe Ile Val Arg Phe Leu Glu Ser Asn Trp Phe Val Trp
                325                 330                 335
Val Thr Gln Met Asn His Ile Pro Met His Ile Asp His Asp Arg Asn
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        355                 360                 365
Ser Ala Phe Asn Asp Trp Phe Ser Gly His Leu Asn Phe Gln Ile Glu
    370                 375                 380
His His Leu Phe Pro Thr Met Pro Arg His Asn Tyr His Lys Val Ala
385                 390                 395                 400
Pro Leu Val Gln Ser Leu Cys Ala Lys His Gly Ile Glu Tyr Gln Ser
                405                 410                 415
Lys Pro Leu Leu Ser Ala Phe Ala Asp Ile Ile His Ser Leu Lys Glu
            420                 425                 430
Ser Gly Gln Leu Trp Leu Asp Ala Tyr Leu His Gln
        435                 440
```

Fig. 7

FADS2

```
Met Gly Lys Gly Gly Asn Gln Gly Glu Gly Ala Ala Glu Arg Glu Val
1               5                   10                  15

Ser Val Pro Thr Phe Ser Trp Glu Glu Ile Gln Lys His Asn Leu Arg
            20                  25                  30

Thr Asp Arg Trp Leu Val Ile Asp Arg Lys Val Tyr Asn Ile Thr Lys
        35                  40                  45

Trp Ser Ile Gln His Pro Gly Gly Gln Arg Val Ile Gly His Tyr Ala
    50                  55                  60

Gly Glu Asp Ala Thr Asp Ala Phe Arg Ala Phe His Pro Asp Leu Glu
65                  70                  75                  80

Phe Val Gly Lys Phe Leu Lys Pro Leu Leu Ile Gly Glu Leu Ala Pro
                85                  90                  95

Glu Glu Pro Ser Gln Asp His Gly Lys Asn Ser Lys Ile Thr Glu Asp
            100                 105                 110

Phe Arg Ala Leu Arg Lys Thr Ala Glu Asp Met Asn Leu Phe Lys Thr
        115                 120                 125

Asn His Val Phe Phe Leu Leu Leu Leu Ala His Ile Ile Ala Leu Glu
    130                 135                 140

Ser Ile Ala Trp Phe Thr Val Phe Tyr Phe Gly Asn Gly Trp Ile Pro
145                 150                 155                 160

Thr Leu Ile Thr Ala Phe Val Leu Ala Thr Ser Gln Ala Gln Ala Gly
                165                 170                 175

Trp Leu Gln His Asp Tyr Gly His Leu Ser Val Tyr Arg Lys Pro Lys
            180                 185                 190

Trp Asn His Leu Val His Lys Phe Val Ile Gly His Leu Lys Gly Ala
        195                 200                 205

Ser Ala Asn Trp Trp Asn His Arg His Phe Gln His His Ala Lys Pro
    210                 215                 220

Asn Ile Phe His Lys Asp Pro Asp Val Asn Met Leu His Val Phe Val
225                 230                 235                 240

Leu Gly Glu Trp Gln Pro Ile Glu Tyr Gly Lys Lys Lys Leu Lys Tyr
                245                 250                 255

Leu Pro Tyr Asn His Gln His Glu Tyr Phe Phe Leu Ile Gly Pro Pro
            260                 265                 270

Leu Leu Ile Pro Met Tyr Phe Gln Tyr Gln Ile Ile Met Thr Met Ile
        275                 280                 285
```

Fig. 7 cont.

```
Val His Lys Asn Trp Val Asp Leu Ala Trp Ala Val Ser Tyr Tyr Ile
    290                 295                 300

Arg Phe Phe Ile Thr Tyr Ile Pro Phe Tyr Gly Ile Leu Gly Ala Leu
305                 310                 315                 320

Leu Phe Leu Asn Phe Ile Arg Phe Leu Glu Ser His Trp Phe Val Trp
                325                 330                 335

Val Thr Gln Met Asn His Ile Val Met Glu Ile Asp Gln Glu Ala Tyr
            340                 345                 350

Arg Asp Trp Phe Ser Ser Gln Leu Thr Ala Thr Cys Asn Val Glu Gln
        355                 360                 365

Ser Phe Phe Asn Asp Trp Phe Ser Gly His Leu Asn Phe Gln Ile Glu
    370                 375                 380

His His Leu Phe Pro Thr Met Pro Arg His Asn Leu His Lys Ile Ala
385                 390                 395                 400

Pro Leu Val Lys Ser Leu Cys Ala Lys His Gly Ile Glu Tyr Gln Glu
                405                 410                 415

Lys Pro Leu Leu Arg Ala Leu Leu Asp Ile Ile Arg Ser Leu Lys Lys
            420                 425                 430

Ser Gly Lys Leu Trp Leu Asp Ala Tyr Leu His Lys
        435                 440
```

Fig. 8

FADS3

Met Gly Gly Val Gly Glu Pro Gly Pro Arg Glu Gly Pro Ala Gln Pro
1 5 10 15

Gly Ala Pro Leu Pro Thr Phe Cys Trp Glu Gln Ile Arg Ala His Asp
20 25 30

Gln Pro Gly Asp Lys Trp Leu Val Ile Glu Arg Arg Val Tyr Asp Ile
35 40 45

Ser Arg Trp Ala Gln Arg His Pro Gly Gly Ser Arg Leu Ile Gly His
50 55 60

His Gly Ala Glu Asp Ala Thr Asp Ala Phe Arg Ala Phe His Gln Asp
65 70 75 80

Leu Asn Phe Val Arg Lys Phe Leu Gln Pro Leu Leu Ile Gly Glu Leu
85 90 95

Ala Pro Glu Glu Pro Ser Gln Asp Gly Pro Leu Asn Ala Gln Leu Val
100 105 110

Glu Asp Phe Arg Ala Leu His Gln Ala Ala Glu Asp Met Lys Leu Phe
115 120 125

Asp Ala Ser Pro Thr Phe Phe Ala Phe Leu Leu Gly His Ile Leu Ala
130 135 140

Met Glu Val Leu Ala Trp Leu Leu Ile Tyr Leu Leu Gly Pro Gly Trp
145 150 155 160

Val Pro Ser Ala Leu Ala Ala Phe Ile Leu Ala Ile Ser Gln Ala Gln
165 170 175

Ser Trp Cys Leu Gln His Asp Leu Gly His Ala Ser Ile Phe Lys Lys
180 185 190

Ser Trp Trp Asn His Val Ala Gln Lys Phe Val Met Gly Gln Leu Lys
195 200 205

Gly Phe Ser Ala His Trp Trp Asn Phe Arg His Phe Gln His His Ala
210 215 220

Lys Pro Asn Ile Phe His Lys Asp Pro Asp Val Thr Val Ala Pro Val
225 230 235 240

Phe Leu Leu Gly Glu Ser Ser Val Glu Tyr Gly Lys Lys Lys Arg Arg
245 250 255

Tyr Leu Pro Tyr Asn Gln Gln His Leu Tyr Phe Phe Leu Ile Gly Pro
260 265 270

Pro Leu Leu Thr Leu Val Asn Phe Glu Val Glu Asn Leu Ala Tyr Met
275 280 285

Fig. 8 cont.

```
Leu Val Cys Met Gln Trp Ala Asp Leu Leu Trp Ala Ala Ser Phe Tyr
    290                 295                 300

Ala Arg Phe Phe Leu Ser Tyr Leu Pro Phe Tyr Gly Val Pro Gly Val
305                 310                 315                 320

Leu Leu Phe Phe Val Ala Val Arg Val Leu Glu Ser His Trp Phe Val
                325                 330                 335

Trp Ile Thr Gln Met Asn His Ile Pro Lys Glu Ile Gly His Glu Lys
            340                 345                 350

His Arg Asp Trp Val Ser Ser Gln Leu Ala Ala Thr Cys Asn Val Glu
        355                 360                 365

Pro Ser Leu Phe Thr Asn Trp Phe Ser Gly His Leu Asn Phe Gln Ile
    370                 375                 380

Glu His His Leu Phe Pro Arg Met Pro Arg His Asn Tyr Ser Arg Val
385                 390                 395                 400

Ala Pro Leu Val Lys Ser Leu Cys Ala Lys His Gly Leu Ser Tyr Glu
                405                 410                 415

Val Lys Pro Phe Leu Thr Ala Leu Val Asp Ile Val Arg Ser Leu Lys
            420                 425                 430

Lys Ser Gly Asp Ile Trp Leu Asp Ala Tyr Leu His Gln
        435                 440                 445
```

Fig. 9

Oligonucleotide primers to amplify FADS1 cDNA

TU12-R5 (5'-CGCCTGACAGCCCCTGCT-3')
TU12-F10 (5'-CAGGTGGCCAATCACAAAAT-3')

TU12-R7 (5'-CTCAAAGTGGAACCATCTGCTA-3')
TU12-F9 (5'-GGAAACCCAGTCCATGTTCC-3')

TU12-R6 (5'-CCTGGGCCTTTTCTTCATAGT-3')
TU12-F5 (5'-CTCAAGCTCCCCTCTGCCT-3')

Oligonucleotide primers to amplify FADS2 cDNA

TU13-R4 (5'-TCAGAAGCATAACCTGCGC-3')
TU13-F7 (5'-CCAGTTCACCAATCAGCAGG-3')

TU13-R3 (5'-CCCCTGCTGATTGGTGAACT-3')
TU13-F4 (5'-TGTAGGGCAGGTATTTCAGC-3')

TU13-R2 (5'-AGCCCATCGAGTACGGCAA-3')
TU13-F1 (5'-CCTCAGAACAAAAGCCCATC-3')

Oligonucleotide primers to amplify FADS3 cDNA

TU19-R2 (5'-TCTTGCTCGGACCTCGGC-3')
TU19-F2 (5'-GTGATCCACACGAACCAGTG-3')

TU19-R3 (5'-GAAGAACCCAGCCAGGATG-3')
TU19-F3 (5'-ACAGCTTTCCCCCAATTCTC-3')

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

Application Number EP 99 10 4664

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	"AC AI394672" EMBL DATABASE, 5 February 1999 (1999-02-05), XP002111712 Heidelberg * the whole document *	1-12	C12N15/53 C12N15/11 C12N15/85 C12N9/02 C12N5/10 C12Q1/02 C07K16/40 A61K39/395 A61K38/44 A01K67/027 G01N33/50 G01N33/53
X	WO 98 46763 A (THURMOND JENNIFER ;CALGENE LLC (US); ABBOTT LAB (US); KNUTZON DEBO) 22 October 1998 (1998-10-22) * see esp. SEQ ID NOs: 27-40	1-12,17, 18	
X	CHO H P ET AL: "Cloning, expression, and nutritional regulation of the mammalian Delta-6 desaturase." JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 JAN 1) 274 (1) 471-7. , XP002111713 * the whole document *	1-12,17, 18	
X	"AC 060426" EMBL DATABASE,1 August 1998 (1998-08-01), XP002111714 Heidelberg * the whole document *	7-10	TECHNICAL FIELDS SEARCHED (Int.Cl.7) C12N C12Q C07K A61K A01K G01N
	-/--		

INCOMPLETE SEARCH

The Search Division considers that the present application, or one or more of its claims, does/do not comply with the EPC to such an extent that a meaningful search into the state of the art cannot be carried out, or can only be carried out partially, for these claims

Claims searched completely :

Claims searched incompletely

Claims not searched :

Reason for the limitation of the search:

see sheet C

Place of search	Date of completion of the search	Examiner
THE HAGUE	10 August 1999	Kania, T

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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European Patent Office

INCOMPLETE SEARCH
SHEET C

Application Number
EP 99 10 4664

Although claim 17 is directed to a method of treatment of the human/animal body (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the compound/composition.

Claim(s) searched incompletely:
16

Reason for the limitation of the search:

Claims 14 and 15 were only interpreted and searched with reference to the use of the present molecules and vectors in these assays.
Claim 16 could not be searched completely due to the lack of characterization of the claimed subject matter.

European Patent Office

Application Number
EP 99 10 4664

CLAIMS INCURRING FEES

The present European patent application comprised at the time of filing more than ten claims.

- [ ] Only part of the claims have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims and for those claims for which claims fees have been paid, namely claim(s):

- [ ] No claims fees have been paid within the prescribed time limit. The present European search report has been drawn up for the first ten claims.

LACK OF UNITY OF INVENTION

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

see sheet B

- [ ] All further search fees have been paid within the fixed time limit. The present European search report has been drawn up for all claims.

- [X] As all searchable claims could be searched without effort justifying an additional fee, the Search Division did not invite payment of any additional fee.

- [ ] Only part of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the inventions in respect of which search fees have been paid, namely claims:

- [ ] None of the further search fees have been paid within the fixed time limit. The present European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims, namely claims:

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LACK OF UNITY OF INVENTION SHEET B

Application Number
EP 99 10 4664

The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 1-18 partially

   An isolated polynucleotide selected from the group consisting of
   polynucleotides having at least 65%, preferably 80% homology with a polynucleotide encoding a polypeptide of SEQ ID NO:4, comprising variants, under stringent conditions hybridizing molecules, complementary molecules, and oligonucleotides comprising at least 15 consecutive nucleotides of said sequence, preferably the polynucleotide of SEQ ID NO:1.
   Vectors, host cells, and transgenic organisms comprising said sequences.
   A polypeptide comprising a sequence having at least 65%, more preferably 85% homology to SEQ ID NO:4, variants thereof, and a peptide comprising at least 15 consecutive amino acids thereof. A process for producing said polypeptide using said host cells and DNA sequences.
   Antibodies against said polypeptides, and their use in diagnosis and therapy.
   An oligonucleotide primer having a sequence selected from the group of nucleotide sequences of SEQ ID NOs:7-12.
   A method of screening for modulators in known assays using constructs or of screening for interacting proteins or factors using state of the art technologies, as well as a method of screening chemical libraries comprising transformed cell lines, both methods employing the said sequences, vectors, or host cells.
   A compound which alters or reacts with at least one epitope of the proteins and which is obtained by said methods.
   Pharmaceutical compositions comprising as an effective component an effective amount of said peptides.

2. Claims: 1-18 partially

   idem for SEQ ID NOs:2,5,13-18

3. Claims: 1-18 partially

   idem for SEQ ID NOs:3,6,19-22

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number
EP 99 10 4664

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
X	"AC 060427" EMBL DATABASE,1 August 1998 (1998-08-01), XP002111715 Heidelberg * the whole document *	7-10	
A	OLGA SAYANOVA ET AL: "Expression of a borage desaturase cDNA containing an N-terminal cytochrome b5 domain results in the accumulation of hig levels of Delta6-desaturated fatty acids in transgenic tobacco" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 94, no. 94, 15 April 1997 (1997-04-15), pages 4211-4216 4216, XP002106758 ISSN: 0027-8424 * the whole document *	1-18	TECHNICAL FIELDS SEARCHED (Int.Cl.7)
A	MITCHELL, ANDREW G. ET AL: "A novel cytochrome b-5-like domain is linked to the carboxyl terminus of the Saccharomyces cerevisiae DELTA-9 fatty acid desaturase." JOURNAL OF BIOLOGICAL CHEMISTRY, (1995) VOL. 270, NO. 50, PP. 29766-29772 , XP002111716 * the whole document *	1-18	
A	WO 96 02561 A (GEN HOSPITAL CORP ;GENETICS INST (US)) 1 February 1996 (1996-02-01) * the whole document *	14,16	
A	WO 99 04262 A (MYELOS NEUROSCIENCES CORP) 28 January 1999 (1999-01-28) * see esp. claims *	15,16	

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ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 99 10 4664

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
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10-08-1999

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9846763 A	22-10-1998	AU 6961698 A	11-11-1998
		AU 7114798 A	11-11-1998
		WO 9846764 A	22-10-1998
WO 9602561 A	01-02-1996	EP 0773952 A	21-05-1997
		JP 10504713 T	12-05-1998
WO 9904262 A	28-01-1999	AU 8480798 A	10-02-1999

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